



Effect of NaCl and KCl on the Micellization of Sodium Dodecyl Sulfate and Sodium Dodecyl Benzene Sulfonate in presence of Cephadrine Monohydrate Through Conductivity

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ABSTRACT

The effect of NaCl and KCl on the micellization of sodium dodecyl sulfate (SDS) and sodium dodecyl benzene sulfonate (SDBS) surfactants in cephadrine monohydrate (CPDM) has been studied by conductance measurement. In this study, we have examined the critical micelle concentration (CMC) of surfactant solutions in drug-salt systems by conductance measurement in an aqueous medium and electrolyte solutions. In this study, CMC were calculated through piece-wise linear model by identifying a distinct and abrupt change in the specific conductivity (G) as the surfactant concentration increased. In all the experimental cases examined, a single CMC was identified for both the CPDM+SDS and CPDM+SDBS systems. The presence of CPDM in an aqueous solution decreases the critical micelle concentration (CMC) of surfactants, thereby increasing the degree of micellization. The CMC values were found to favorable with an increase of salt NaCl and KCl concentrations. And very tremendously different results were found between CPDM+SDS/SDBS and CPDM+SDS/SDBS+KCl and CPDM+SDS/SDBS+NaCl systems. The result shows very remarkable information about the micellization of surfactants in the presence of drug and salt solutions.

Keywords: Micelle, CMC, Specific Conductivity, Micelle ionization Value.

INTRODUCTION

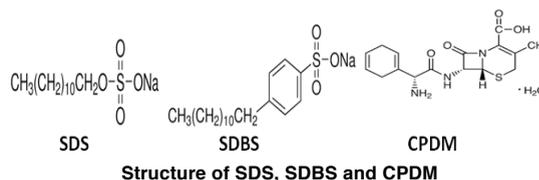
Compounds known as surfactants are made up of lyophilic groups that have a high affinity to the solvent and lyophobic groups that have a very weak one. Such types of structures are called amphiphatic compounds^{1,2}. Surfactants have different uses in textiles, cosmetic and domestic products, metal extraction, food processing, nanotechnologies, oil recovery, and pharmaceuticals

for hydrophobic drug solubilization in aqueous phase, as parts of emulsions, plasticizers in semisolid delivery systems, surfactant micelle vehicles for transdermal and oral drug delivery, and as agents to improve drug absorption and penetration^{3,4}. The surfactant molecules form very well ordered micelles, bi-layers, hexagonal, monolayers, or cubic phases that aggregate themselves⁵⁻⁷. These different phases are affected by the structure of surfactants, the space gap between the hydrophilic and hydrophobic



parts and the extent of hydrophilic-hydrophobic balance. The process of inter-conversion occurs depending on factors such as the pH of the medium, temperature, and ionic strength⁷⁻⁹. The critical micelle concentration (CMC) represents the concentration level at which micellar structures begin to form^{7,10}. In the micelle, the micelle core part contains the non-polar moieties portion and outside part contains the polar part of the surfactant molecule⁷. Then they are arranged by solvent as a spherical arrangement for both the anionic and cationic surfactant micelles at CMC^{11,12}. The ionic surfactants improve drug permeability through the skin¹³.

The surfactants can be used in their micellized form for feebly soluble drugs to increase the dissolution rate¹³. The membrane function is affected by surfactants and the absorption, and penetration of drugs across the gastrointestinal wall are improved by the surfactants^{13,14}. Surfactants have a better performance in terms of absorption and release of drugs in the blood stream in micellar form¹⁴⁻¹⁹. Because of the similarity between the surfactant micelle and the biological membrane, this concept of micelle formation could prove beneficial for studying the different modes in which the chosen drugs bind²⁰. As the micelles have a very stable structure and have an appropriate size, they can congregate easily in the targeted areas²¹.



Cephadrine is a first-generation cephalosporin and beta-lactam antibiotic²². It effectively combats both *Gram-positive* and *Gram-negative* bacteria. Its application spans across treating upper respiratory tract infections, lower respiratory tract infections, urinary tract infections, as well as skin and soft tissue infections²³. SDS is an anionic surfactant²⁴. It is used in our everyday items, such as foods, pharmaceutical formulations, cleaning agents, and research purposes also²⁵⁻²⁷. SDBS is also an anionic surfactant. It is well known as a surface active compound. It is used in chemical, biochemical, and industrial work. It shows antifungal properties^{28,29}. As NaCl and KCl is naturally found in the human body and sometimes NaCl is pushed along with glucose solutions, so they may affect the physicochemical interaction of membranes with drugs^{7,30}. A number of studies on the interaction with drug molecules have been reported in the literature^{16,21} but for our best knowledge, it is necessary to explore the interactions of cephadrine on the micellization of SDS and SDBS in the presence of NaCl and KCl³¹.

Table 1: Specifications of Chemicals

Chemical name	Molar mass/kg.mol ⁻¹	Purity declared by supplier	origin
Cephadrine monohydrate(CPDM)	0.34941	0.995	SKF pharmaceuticals Ltd
Sodium dodecyl sulfate(SDS)	0.28838	0.990	Merck(Germany)
Sodium Chloride(NaCl)	0.05844	0.995	Merck in Germany
Potassium Chloride(KCl)	0.07455	0.995	Merck in Germany

MATERIALS AND METHOD

Materials

All the materials utilized in this experiment were analytical reagent grade and were used without any purification. The surfactants, SDS and SDBS were collected from Merck(Germany). The employed drug Cephadrine (Micronised) was collected from SKF Pharmaceuticals Ltd. in Bangladesh. The sodium chloride (NaCl) was acquired from a research lab in India, while potassium chloride (KCl) was procured from Merck in Germany. All solutions were made using deionized water with a specific conductivity lower than 2 μScm^{-1} .

Method

The specific conductivity of CPDM+

$\text{H}_2\text{O} + \text{SDS}$, $\text{CPDM} + \text{H}_2\text{O} + \text{SDS} + \text{NaCl/KCl}$, $\text{CPDM} + \text{H}_2\text{O} + \text{SDBS}$, $\text{CPDM} + \text{H}_2\text{O} + \text{SDBS} + \text{NaCl/KCl}$ systems were measured through Hanna EC/TDS/Salinity Benchtop Meter-HI2550 having a cell constant 1 cm^{-1} and an accuracy of $\pm 0.05 \mu\text{Scm}^{-1}$. The FA2204 analytical balance was used for weight measurements. All the experiments were performed at 25°C, which was controlled by the shaking water bath model SHWB-30. The experiment was conducted according to the procedure outlined in the literature^{29,32,33}.

The stock solutions of SDS(0.15mol/kg) and SDBS(0.15 mol/kg) were prepared by solvent-1,2 and 3 (solvent-1(CPDM+H₂O), solvent-2(CPDM+H₂O+NaCl), solvent-3(CPDM+H₂O+KCl)), and then the SDS and SDBS solutions were transferred

gradually into a beaker containing the corresponding 80 g solvent-1,2 and 3 for targeting the desired concentration. After adding the SDS/SDBS solution every time it was mixed properly. A conductivity meter was used to measure the values of G and each time a stock solution of surfactants was added to the solvent. Plotting of the G values versus the corresponding surfactant concentrations has been done.

RESULTS AND DISCUSSION

Conductometric study is one of the basic structurally susceptible methods for analysis aggregation or micellar systems and this method is widely applied to evaluate critical micelle concentrations (CMCs). As the concentration of an ionic surfactant rises within a solution, a change is noticeable in the conductivity data curve near the critical micelle concentration (CMC). Beyond this point, the increase in conductivity becomes less pronounced, indicating a slower rate of change. This occurrence is attributed to the reduced mobility of micelles in an electric field compared to unassociated surface-active ions due to their larger size. Some graphs of the specific conductivity of SDS and SDBS in aqueous, CPDM+H₂O, CPDM +H₂O+NaCl, and CPDM+H₂O+KCl solutions are graphically represented in Fig. 1, 3 and the second derivatives are presented graphically in Figures 2, 4.

To determine the critical micelle concentration (CMC) precisely, the conductance value as a function of molality was fitted to the following piece-wise linear model;

$$G = \begin{cases} A + b_1 m, & m \leq CMC \\ A + b_1 X + b_2 (m - CMC), & m \geq CMC \end{cases} \quad (1)$$

Where A indicates the intercepts, ($m \rightarrow 0; G \rightarrow A$), b_1 and b_2 refer to the experimental slopes in the before and after-CMC regions, respectively. Table 2 contains the values of the fitting parameters accompanied by their respective standard uncertainties, and CMC's are graphically shown in Fig. 5, 6 against the concentrations of NaCl and KCl. The conductivity values are calculated using eq (4.1). The second derivative data follows the Gaussian peak function, which indicates the existence of a breaking point in conductivity versus molality data. The degree of dissociation of micelle $\beta = b_1/b_2$ and the degree of association of micelle $\alpha = (1-\beta)$, were calculated in the pre- and post-CMC regions. The values of α and β offer significant physicochemical insights into the properties of the surfactant micelle³⁴.

The conductivity of all systems was

observed to progressively rise as the concentration of surfactant increased (Fig. 1,3). Because ionic surfactants like SDS and SDBS get dissociated and produce surfactant ions and counter ions. These ions are responsible for conductivity. As the concentration increases, the number of ions increases, resulting in higher conductivity. But after a definite concentration, surfactant ions get self-assembled and then conductivity increases at a slower rate. In this specific concentration, the plot of surfactant concentration vs. conductivity shows a breakpoint at CMC. In all our experiments we have obtained only one CMC.

CPDM+SDS and CPDM+SDBS have CMC values that are less than those of pure SDS and SDBS in water, indicating that the addition of CPDM promotes the formation of surfactant micelles. For both SDS and SDBS, the CMC values dropped as NaCl and KCl concentrations increased (Fig. 5, 6). Thus, the CPDM supported surfactant micelles are stabilized by the addition of NaCl and KCl. The term "salting effect" refers to the phenomenon wherein CMC values decrease when neutral salts such as NaCl and KCl are added^{7,16}. Other research teams have similarly noted a decrease in the CMC when electrolytic salts are introduced during the micellization process involving interactions between ionic surfactants and drug surfactants³⁵⁻³⁷. Both NaCl and KCl are potent electrolytes. By complete dissociation, they release Cl⁻ ions and water structure become stable by solvating Cl⁻ ions, this leads to a significant salting-out effect on the hydrophobic portion of the surfactant monomer. The existence of NaCl and KCl aids in neutralizing surface charges, thereby reducing repulsion between head groups and promoting micelle formation^{5,7}. In comparison to NaCl and KCl, CMC decreases more when KCl is present and less when NaCl is present for both SDS and SDBS Fig. 9, 10. The van der Waals radius (R) and valence (Z) ratio can be used to describe it. Larger Z/R cations are more hydrated and contribute more water structure³⁶. Because these ions can salt out the hydrophobic groups of the surfactants in the aqueous phase, they have a greater effect on the CMC value. In the presence of KCl, there is a greater drop in CMC because the Z/R value for K⁺ ions is higher³⁸.

From the slope before (S_b) and after (S_a) CMC, α values can be obtained using the equation, $\alpha = S_a/S_b$, and β values can be computed from the relation $\beta = 1-\alpha$. Important physicochemical features of the surfactant micelle are provided by the values of α and β . In our current study we have a good

agreement with references¹⁶. The lower alpha values observed for CPDM+SDS indicate that it exhibits weaker interaction with SDS micelles, resulting in less efficient solubilization compared to SDBS micelles³².

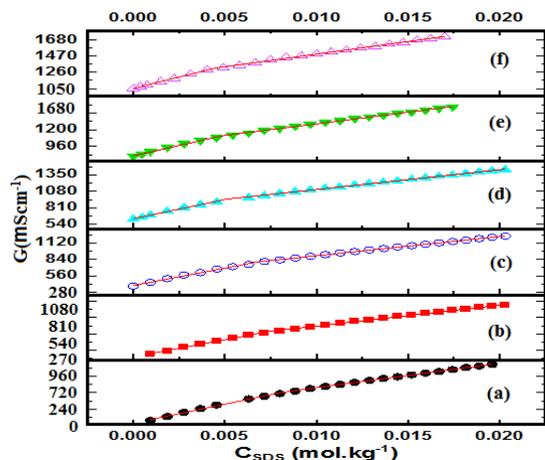
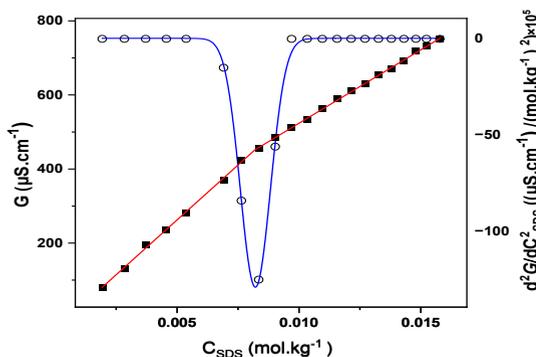
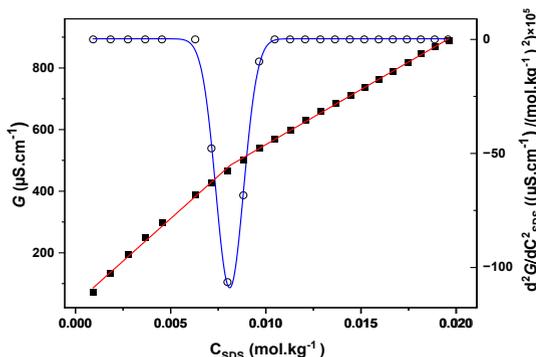


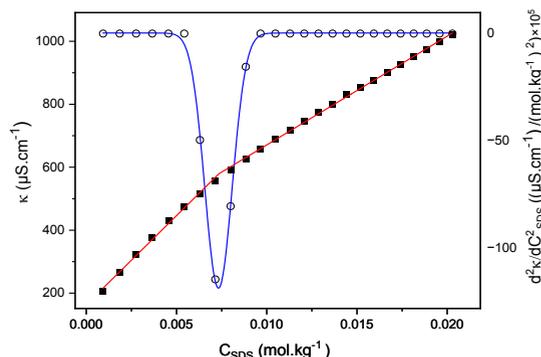
Fig. 1. Conductivities of (a) SDS+water+CPDM(0.001 mol/kg), (b) SDS+water+ NaCl(0.001 mol/kg)+CPDM(0.001 mol/kg), (c) SDS+water+NaCl(0.003 mol/kg)+CPDM(0.001 mol/kg), (d) SDS+water+NaCl(0.005 mol/kg)+CPDM(0.001 mol/kg), (e) SDS+water+NaCl(0.007 mol/kg) +CPDM(0.001 mol/kg), (f) SDS+water+NaCl(0.009 mol/kg)+CPDM(0.009 mol/kg) systems as a function of molality of SDS at 295.15 K.



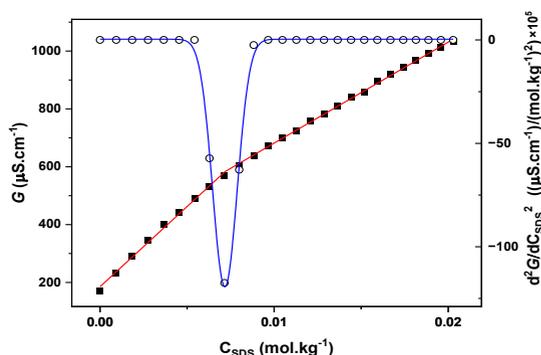
(a) SDS+water



(b) SDS+water+cephradine



(c) SDS+water+NaCl(0.001 mol/kg)+CPDM(0.001 mol/kg)



(d) SDS+water+KCl(0.001 mol/kg)+CPDM(0.001 mol/kg)

Fig. 2. Conductivities of (a) SDBS+water, (b) SDBS+water+CPDM(0.001 mol/kg), (c) DS+water+NaCl(0.001 mol/kg)+CPDM(0.001 mol/kg) and (d) SDS+water+KCl(0.001 mol/kg)+CPDM(0.001 mol/kg) systems (α -Represent experimental and solid line fitting data; β -Second Derivative of fitted data: Solid line fitted data to Gaussian function)

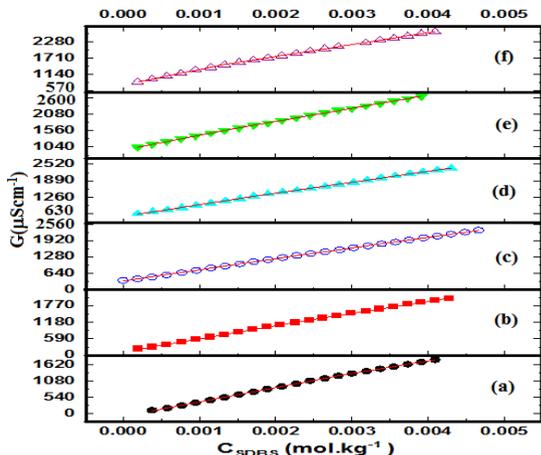


Fig. 3. Conductivities of (a) SDBS+water+CPDM(0.001 mol/kg), (b) SDBS+water+ NaCl(0.001 mol/kg)+CPDM(0.001 mol/kg), (c) SDBS+water+NaCl(0.003 mol/kg)+CPDM(0.001 mol/kg), (d) SDBS+water+NaCl(0.005 mol/kg)+CPDM(0.001 mol/kg), (e) SDBS+water+NaCl(0.007 mol/kg) +CPDM(0.001 mol/kg) (f) SDBS+water+NaCl(0.009 mol/kg)+CPDM(0.009 mol/kg) systems as a function of molality of SDS at 295.15 K

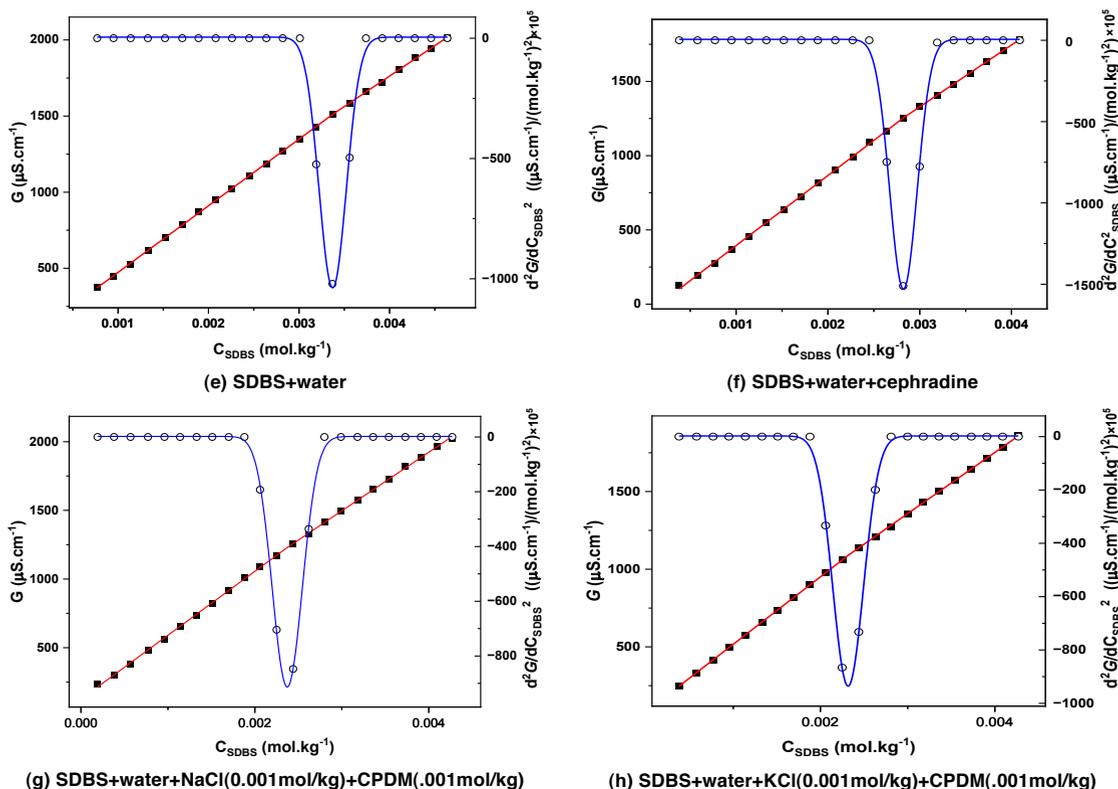


Fig. 4. Conductivities of (e) SDBS+water, (f) SDBS+water+CPDM(0.001mol/kg), (g) SDBS+water+NaCl(0.001mol/kg)+CPDM (0.001mol/kg) and (h) SDBS+water+KCl(0.001mol/kg)+CPDM(0.001mol/kg) systems (α -Represent experimental and solid line fitting data; β -Second Derivative of fitted data; Solid line fitted data to Gaussian function)

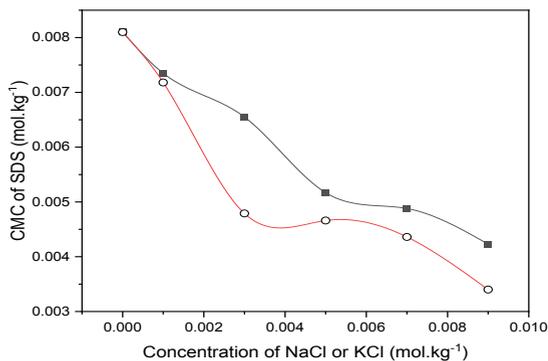


Fig. 5. CMC of SDS in Cephadrine (.001mol/kg)+NaCl/KCl systems(α -Represents CMC in presence of NaCl and β -represents CMC in presence of KCl)

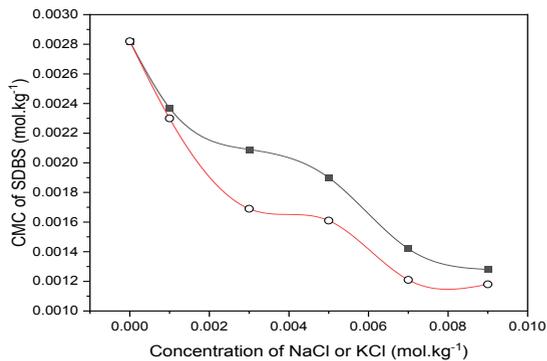


Fig. 6. CMC of SDBS in Cephadrine(0.001mol/kg)+NaCl/KCl systems(α -Represents CMC in presence of NaCl and β -represents CMC in presence of KCl)

Table 2: Critical micelle concentration, CMC of SDS and SDBS in water and in Water+NaCl/KCl+CDPM solutions

Systems	CMC(X)(m/mol.kg ⁻¹)		α	β
SDS+Water	0.00819		0.67011	0.32989
SDBS+Water	0.00337		0.91377	0.08623
m (mol.kg ⁻¹) of NaCl	CMC of SDS in Cephadrine (0.001mol/kg) +NaCl solution	CMC of SDS in Cephadrine (0.001mol/kg) +KCl solution	α SDS+Cephadrine (0.001mol/kg)+NaCl	β SDS+Cephadrine (0.001mol/kg)+KCl

0.000	0.00814	0.00814	0.64770	0.64770	0.3523	0.3523
0.001	0.00735	0.00718	0.61409	0.63011	0.38591	0.36988
0.003	0.00678	0.00540	0.55409	0.63701	0.44591	0.36701
0.005	0.00509	0.00468	0.51438	0.76511	0.48562	0.23849
0.007	0.00481	0.00438	0.56097	0.63360	0.43903	0.3664
0.009	0.00440	0.00352	0.55209	0.37341	0.44791	0.62659

<i>m</i> /(mol·kg ⁻¹) of KCl	CMC of SDBS in Cephadrine (0.001mol/kg) +NaCl solution	CMC of SDBS in Cephadrine (0.001mol/kg) +KCl solution	SDBS+Cephadrine (0.001mol/kg)+NaCl	SDBS+Cephadrine (0.001mol/kg)+KCl	SDBS+Cephadrine (0.001mol/kg)+NaCl	SDBS+Cephadrine (0.001mol/kg)+KCl
0.000	0.00282	0.00282	0.88359	0.88359	0.11641	0.11641
0.001	0.00237	0.00232	0.91648	0.90677	0.08352	0.09323
0.003	0.00209	0.00161	0.94927	0.90369	0.05073	0.09631
0.005	0.00170	0.00154	0.93559	0.91173	0.06441	0.08827
0.007	0.00140	0.00129	0.89436	0.90959	0.10564	0.09041
0.009	0.00129	0.00103	0.77913	0.86314	0.22087	0.13686

CONCLUSION

A comprehensive conductometric study was conducted to investigate the interaction between the antibiotic CPDM and the anionic surfactants SDS and SDBS, both in aqueous solutions and in salt solutions. A significant interaction between the drug and surfactants was observed in the presence of the salts NaCl and KCl when each was added independently. Our results indicate that the interaction between the drug and SDS, SDBS is due to strong hydrophobic interactions. The CMC values of the surfactants were consistently lower than the ideal CMC values, with these values further decreasing in the presence of NaCl and KCl. The reduction in CMC as the concentration of KCl or NaCl rises is ascribed to the diminished electrostatic repulsion between the charged head groups of surfactants in the

presence of CDM, thereby promoting the creation of surfactant micelles. In comparison to NaCl, there was a greater decrease in CMCs when KCl was present. We can learn more about the nature of the drug-surfactant interaction thanks to the data. It can be extremely important for both medication delivery systems and improved drug formulation.

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Conflict of interest

The author declare that we have no conflict of interest.

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